

PATENT

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

**Application No. :** 10/536,853  
**Applicant :** AZNAR, Pascal  
**Filing Date :** 2005-05-27  
**Confirmation No.:** 4377  
**Art Unit :** 4116  
**Examiner :** MARTINEZ, Brittany M  
**Docket No. :** 103.001  
**Customer No. :** 41754

Mail Stop Amendments  
Commissioner for Patents  
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**AMENDMENT AND RESPONSE UNDER 37 CFR 1.115**  
**(SUBMITTED AS INFORMAL DRAFT)**

Dear Sir:

In response to the Office Action of December 17, 2009 with a period for response extended to expire after May 17, 2010, please amend the above-identified application as follows.

**Amendments to the Claims** are reflected in the listing of claims which begins on page 2 of this paper.

**Remarks/Arguments** begin on page 5 of this paper.

Each section begins on a separate sheet in accordance with the revised format practice.

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### **Amendments to the claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

### **Listing of Claims:**

1. (cancel)
2. (cancel)
3. (Currently Amended) ~~The column for flash chromatography according to claims 1 or 2~~ Claim 7 or 9 wherein the flash chromatography column contains ~~containing~~ between 10 mg to 1 kg of spherical and porous silica gel ~~or semi-spherical and porous silica gel.~~
4. (Currently Amended) The flash chromatography column ~~for flash chromatography~~ according to claims ~~1 or 2~~ 9 or 10 manufactured with tubes as well as with syringe bodies ~~or similar forms.~~
5. (Currently Amended) The flash chromatography column ~~for flash chromatography~~ according to claim 3 and manufactured with tubes as well as with syringe bodies ~~or similar forms.~~
6. (Currently Amended) ~~A~~ The pre-filled flash chromatography column ~~for flash chromatography~~ according to claims ~~1 or 2~~ 9 or 10 adapted to purify synthetic products in quantities comprised between 10 mg to 100 g.
7. (new) A method for purifying a product comprising:  
  
    performing a flash chromatography process by:  
  
        introducing an eluent with at least one product to be  
            purified into a flash chromatography column  
            pre-filled with a spherical and porous silica gel

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having particle size between 3 and 45  $\mu\text{m}$  and  
pores between 30 and 300 $\text{\AA}$ ;

cause the eluent to flow through the pre-filled column;  
and

obtain a separation of the at least one product to be  
purified.

8. (new) A method for purifying a product comprising:

performing a flash chromatography process by:

introducing an eluent with at least one product to be  
purified into a flash chromatography column  
pre-filled with a semi-spherical and porous  
silica gel having particle size between 3 and 45  
 $\mu\text{m}$  and pores between 30 and 300 $\text{\AA}$ ;

cause the eluent to flow through the pre-filled column;  
and

obtain a separation of the at least one product to be  
purified.

9. (new) A pre-filled flash chromatography column for purifying a product,  
comprising

a plastic or glass tube or syringe body; and

spherical and porous silica gel having particle size between 3  
and 45  $\mu\text{m}$  and pores between 30 and 300 $\text{\AA}$  placed  
inside the flash chromatography tube.

10. (new) A pre-filled flash chromatography column for purifying a  
product, comprising

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a plastic or glass tube or syringe body; and  
semi-spherical and porous silica gel having particle size  
between 3 and 45  $\mu\text{m}$  and pores between 30 and 300Å  
placed inside the flash chromatography tube.

11. (New) Claim 8 or 10 wherein the flash chromatography column  
contains between 10 mg to 1 kg of semispherical and porous silica gel.

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## **Remarks:**

### **Status of the Claims**

In the Office Action mailed on December 17, 2009, the Examiner rejected claims 1-6. Claims 1 and 2 are cancelled herein. Claims 3 – 6 are amended herein. New Claims 7 through 11 are added herein. Claims 3 through 11 are now pending in the application.

New Claims 7 and 8 are directed to a method for purifying a product by performing a flash chromatography process using a flash chromatography column pre-filled with a spherical and porous silica gel having particle size between 3 and 45  $\mu\text{m}$  and pores between 30 and 300 $\text{\AA}$ . The purification of a product in aforementioned manner is described in the specification, at least, for example, as Example 1 and results obtained (Specification, Page 2, Line 27 – Page 3, Line 14). Thus, no new matter has been added in the introduction of these claims.

New Claims 9 and 10 have been amended to recite “a plastic or glass tube” into which “spherical (Claim 9)” or “semi-spherical (Claim 10)” “and porous silica gel having particle size between 3 and 45  $\mu\text{m}$  and pores between 30 and 300 $\text{\AA}$ ” is placed. Dr. Domingo Sanchez, in a declaration co-filed herewith, has declared and submitted prior art evidence showing that a person of ordinary skill in the art would typically employ a glass or plastic tube or syringe body to construct a flash chromatography column. Therefore, no new matter is introduced by these claims.

### **Interview Summary**

An interview was held on March 8, 2010. The examiner's Interview Summary accurately reflects the substance of the interview, and is incorporated herein by reference. Applicant gave a presentation of his inventive technology in the context of the prior art. Applicant and the Examiners discussed various different approaches to claiming the

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invention. The Examiners suggested an amendment of the claims as set out herein above which the Applicant agreed to. The Examiners further requested and the Applicant agreed to that Applicant would provide a declaration under 37 CFR 1.132 providing evidence of the differences in the columns used in flash chromatography and in high-performance liquid chromatography.

A telephonic interview was held on April 5, 2010 in which Examiners Brittany Martinez and Wayne Langel participated for the USPTO and the undersigned for the Applicant. Applicant agrees with the Interview Summary filed by the Examiners and it is incorporated herein by reference.

A second telephone interview was held on April 9, 2010 with the same participants. The participants discussed new proposed claim amendments and new claims transmitted by the undersigned in draft on April 6, 2010. The claims then-transmitted and discussed are largely as those provided herein other than two claims discussed in the interview and that attempted to avoid the limitation of specific materials for the tube or syringe used in favor of a general limitation to tube or syringe have not been included herein. The Examiners indicated that such combinations would likely read on the prior art. Applicants agreed to not present those claims in the formal reply. Applicants indicated that a response would be filed including a declaration showing that one of ordinary skill in the art would typically employ a plastic or glass tube for flash chromatography.

Applicant and Applicant's undersigned representative thank the Examiners for granting the in person interview and spending time discussing the prior art of record and the claimed invention, as well as subsequent telephonic interviews.

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## **The Claims**

### **35 USC 112, second paragraph**

Claims 4 and 5 stand rejected under 35 USC 112, second paragraph because it was deemed that the meaning of “similar forms” was unclear. Applicants have amended the claims to remove this language. Accordingly, Applicants respectfully request withdrawal of the rejection and allowance of the claims.

### **35 USC 103**

Claims 1-6 were rejected under 35 U.S.C. 102 and 35 U.S.C. 103(a) as unpatentable over a variety of references taken from the High-Performance Liquid Chromatography (HPLC) and Solid Phase Extraction (SPE) arts. The differences between the prior art of record and the claimed invention were discussed at length in the interview of March 8, 2010. Applicant has amended the claims to clarify the scope of the invention. As amended, the claims are not obvious over the prior art as is discussed herein below.

To the extent the Examiner considers the rejection applicable to the claims as amended and the new claims, Applicant traverses the rejection.

Analysis of the prior art references will be facilitated by a brief summary of the technology introduced by and claimed by the Applicant. Keeping in mind that the precise scope of each claim is only limited by the specific limitations of each claim, respectively, Applicant claims methods of performing flash chromatography and pre-filled flash chromatography columns comprising the following features:

- flash chromatography column, i.e., a plastic or glass tube suitable for performing flash chromatography processes in the pressure range encountered in flash chromatography, i.e., up to approximately 10 bars

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- the column is pre-filled with spherical or semi-spherical silica gel
- particle size in the range of 3 to 45  $\mu\text{m}$

Thus, in terms of the solid phase of the claimed flash chromatography columns and method, the following may be stated: the solid phase is:

- shape: spherical or semi-spherical
- material: silica gel
- particle size: in the range of 3 to 45  $\mu\text{m}$

For the first of these (shape), it is important to consider that silica particles may be categorized as *irregular* shaped or, as here, spherical or semi-spherical. Prior art references that teach or suggest *irregular* shaped silica particles do not read on the present invention.

For the second (material): it is important to contrast between raw silica and bonded silica. Silica may be used as a support material for solid phase materials that are bonded with other molecular structures to form the packing material for the solid phase. Examples, include silica bonded with octadecylsilane (see e.g., Williams, US 5,559,039, Col. 2, Lines 4 – 7). The use of bonded silica does not read on the present invention.

For the third (particle size), it is noteworthy that in combination with the shape and material selection, the prior art does not teach or suggest the use of the claimed size range in flash chromatography columns as set forth in the claims.

None of the references, in any combination, teach or suggest the limitations of the claims.

Williams (US 5,559,039) (2 – 5, 31 – 33, 38 – 41)

Claims 1, 2, 3, 4, 5 and 6 were rejected under 35 USC 102(b) or, in the alternative, under 35 USC 103(a) as unpatentable over Williams.



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New claims 7 and 8 are directed to a method for purifying a product comprising performing a flash chromatography process using a flash chromatography column pre-filled with a spherical (Claim 7) or semi-spherical (Claim 8) silica gel having a particle size between 3 and 45  $\mu\text{m}$ . Claims 9 and 10 are directed to a pre-filled flash chromatography column comprising a plastic or glass tube filled with spherical (Claim 9) or semi-spherical (Claim 10) silica gel having a particle size between 3 and 45  $\mu\text{m}$ . Williams does not teach or suggest such limitations.

Williams is directed to high-performance liquid chromatography (HPLC) systems:

“The present invention relates to packing materials for liquid chromatographic or catalytic columns, and more particularly it relates to an improved packing material for use in high performance liquid chromatography and to a method for making and using such a packing material.” Williams, Col. 1, Lines 6 – 9, emphasis added.

Furthermore, while Williams does discuss the use of silica gel, Williams does not discuss spherical/semi-spherical silica having a particle size of 3 – 45  $\mu\text{m}$  as the packing material for the columns. Generally Williams discusses a packing material that is a coated bonded silica. For example, Williams states that “prior to treatment in accordance with the present invention the porous silica support may undergo a silation process with, for example an octadecylsilane as is well known” (Williams, Col. 7, Lines 40 – 42). “In all instances, the coating of crosslinked protein covers the external surfaces of the porous silica support overcoating the alky or ketal-blocked-diol or fluoroalkyl or other external phase of the dual zone or mixed phase material” (Williams, Col. 7, Lines 47 – 51).

The Examiner particularly points to Example 1 beginning on Col. 10, Line 55. Applicant infers that it is the particle size disclosed there that drew the Examiner to that particular example. However, reading the example as a whole, one realizes that the material in the example is not

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raw silica as is claimed in the present application. Rather the material there described is a silica treated to impart a ketal blocked diol residue on all surfaces. Thus, the material proposed in Example 1 as a packing material is not silica but rather a material that uses silica as its *support*.

For the foregoing reasons, Williams does not anticipate or render-obvious Claims 7 through 10.

Koh (Journal of Chromatography A) (6 – 11)

Claims 1, 2, and 6 were rejected under 35 USC 102(b) or, in the alternative, under 35 USC 103(a) as unpatentable over Koh. If the Examiner considers the rejection applicable to the claims as amended and the new claims, Applicant traverses the rejection.

Koh applies to HPLC columns. For example, in section 2, Experiments (Page 224, left-hand column, line 20 et seq.), Koh describes equipment that includes a stain-less steel column body with a maximum allowable compression of 100 kg/cm<sup>2</sup> (~1422 PSI). In Section 3 (Page 226, LH Col., Line 3 et seq.), Koh describes pressurization to 90 kg/cm<sup>2</sup> (~1278 PSI).

Koh does not describe using spherical/semi-spherical silica particles. Koh states that four different packing materials for chromatography were used (Koh, page 224, RH Col., Line 12 et seq.). These include Novapak C18, Hyperprep HS-BDS C18, Baker I-130, and un-modified alumina. Each of Novapak C18, Hyperprep HS-BDS C18, and Baker I-130 are octadecyl (C18) bonded silica. The “C18” in the product names refer to octadecyl. Koh states with respect to Baker I-130 “also a chemical bonded octadecyl silica.” Thus, implying that Novapak C18 and Hyperpre HS-BDS C18 are octadecyl bonded silica rather than silica.

For the foregoing reasons Koh does not anticipate or render-obvious Applicant’s claimed invention.

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SUPELCO (Guide to Solid Phase Extraction) (12 – 15)

Claims 1, 2, and 4 were rejected under 35 USC 102(b) or, in the alternative, under 35 USC 103(a) as unpatentable over Supelco. If the Examiner considers the rejection applicable to the claims as amended and the new claims, Applicant traverses the rejection.

SUPELCO refers to Solid Phase Extraction (SPE) materials. The table on Page 2 of Supelco lists materials used for SPE. These materials include silica-based materials, Alumina-based materials, Florisil®-based materials, Graphitized Carbon-based materials, and Resin-based materials. Of all the listed silica-based materials, only LC-Si is listed as a silica gel with no bonded phase. Dr. Domingo Sanchez, in his declaration co-filed herewith, declares and presents evidence that LC-Si is an irregular shaped silica based on his knowledge and examination of marketing materials from Sigma-Aldrich, the supplier of LC-Si. Thus, SUPELCO does not teach or suggest a column that is pre-filled with a spherical/semi-spherical silica gel with a particle size between 3 and 45  $\mu\text{m}$ .

Accordingly, Applicant respectfully submits that SUPELCO does not teach or suggest the invention claimed in Claims 7 through 10 and respectfully request withdrawal of the rejection.

Schwartz (US 5,128,114) (16 – 18)

Claims 1, and 2 were rejected under 35 USC 102(b) or, in the alternative, under 35 USC 103(a) as unpatentable over Schwartz. If the Examiner considers the rejection applicable to the claims as amended and the new claims, Applicant traverses the rejection.

Schwartz describes the manufacture of silica micro-spheres including spheres having an average diameter in the range of 5 to 20  $\mu\text{m}$ . However, Schwartz does not describe the use of such materials in flash chromatography.

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Schwartz does state that the produces micro-spheres are useful as packing material for chromatographic columns. However, there is no mention as to which type of chromatographic columns are intended. Applicant does not claim to have invented silica gel of in the claimed range, but rather, the use of such silica gel in flash chromatography columns. Schwartz could only be read to teach or suggest the use of such materials in flash chromatography through inference. However, such an inference may not be drawn here because Schwartz could be contemplating other chromatography technologies. Because at the time of invention of Schwartz such materials were in use in HPLC, one must infer that Schwartz contemplated use of the materials in HPLC or another chromatography process already using the specific material.

Kanda et al. (US 6,360,589) (19 – 22)

Claims 1, 2 and 4 were rejected under 35 USC 102(b) or, in the alternative, under 35 USC 103(a) as unpatentable over Kanda. If the Examiner considers the rejection applicable to the claims as amended and the new claims, Applicant traverses the rejection.

Kanda applies to a packing material for a pre-focusing column in a liquid chromatograph apparatus. There is no indication in Kanda that Kanda's pre-focusing column or any other piece of equipment of Kanda is constructed using a "plastic or glass tube or syringe body."

Furthermore, Kanda's packing material is not spherical/semi-spherical silica. Rather Kanda discloses that the porous support material may be selected from a group of materials that include silica gel. Kanda, Col. 11, Lines 16 – 19. However, the column packing material is formed by coating the porous support with a silicone polymer. Kanda, Col. 11, Lines 1 – 6. Thus, Kanda's packing material is not "(semi-)spherical and porous silica gel having particle size between 3 and 45  $\mu\text{m}$ ."

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For, at least this reasons, Kanda does not anticipate or render-obvious the claimed invention.

Teraoka et al. (US 5,587,082) (23 – 27, 34 - 37)

Claims 1, 2, 3, 4, 5 and 6 were rejected under 35 USC 102(b) or, in the alternative, under 35 USC 103(a) as unpatentable over Teraoka. If the Examiner considers the rejection applicable to the claims as amended and the new claims, Applicant traverses the rejection.

Teraoka is directed to two separation methods that are referred to therein as Enhanced Partitioning Fractionation (EPF) and High Osmotic Pressure Chromatography (HOPC). There is no indication that these techniques has any applicability to flash chromatography. Furthermore, the packing material is not “spherical/semi-spherical and porous silica gel having particle size between 3 and 45  $\mu\text{m}$ .” Rather, Teraoka describes the packing material as silated silica gels (“All silica gels for both EPF and HOPC were pretreated with trimethylchlorosilane to minimize adsorption of poloymer to the silica surface.” Teraoka, Col. 12, Lines 13-15.).

Furthermore, Teraoka teaches away of using spherical silica. Teraoka indicates that Davisil® silica gel is used (*see*, Teraoka, Examples). Davisil® is an irregular shaped silica (See, Davisil® Media, [http://www.discoverysciences.com/uploadedFiles/Home/MEDIA\\_Davisil.pdf](http://www.discoverysciences.com/uploadedFiles/Home/MEDIA_Davisil.pdf), accessed on April 18, 2010, attached hereto as Exhibit A, emphasis added therein).

Thus, Teraoka does not teach either the use of silica as the packing material or even that spherical silica is used as the precursor used to prepare the packing material.

Matsushita et al. (US 5,559,039) (28 – 30)

Claims 1, 2, and 6 were rejected under 35 USC 102(b) or, in the alternative, under 35 USC 103(a) as unpatentable over Matsushita. If the

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Examiner considers the rejection applicable to the claims as amended and the new claims, Applicant traverses the rejection.

Matsushita discloses a chromatography system uses two series-connected HPLC columns. Example 1 discloses the use of “type ‘HLC-803A.’” Matsushita, Col. 4, Lines 46 – 47. HLC-803A is an HPLC system. *See e.g.,* Chung, Kang-Go, et al., **Nickel(0)-catalyzed asymmetric cross-coupling reactions of allylic compounds with arylboronic acids**, The Royal Society of Chemistry, pp 15 – 19, at 17 (attached hereto as Exhibit B).

Matsushita further is specific about that the columns are stainless steel columns. Col. 4, Lines 54 – 55, and Col. 63 – 64.

Thus, Matsushita teaches away from “a plastic or glass tube or syringe body” both explicitly and in that Matsushita teaches a system that relies on HPLC equipment.

Accordingly, Claims 7 through 10 are patentable over Matsushita.

Watanabe et al. in view of Kamegawa et al. (42 – 43)

Claims 1, and 2 were rejected under 35 USC 103(a) as unpatentable over Watanabe in view of Kamegawa. If the Examiner considers the rejection applicable to the claims as amended and the new claims, Applicant traverses the rejection.

Watanabe teaches the use of gravity chromatography as opposed to flash chromatography. Thus, Watanabe does not teach or suggest “performing a flash chromatography process by: [performing the claimed steps]” as set forth in Claims 7 and 8.

Furthermore, Watanabe does not teach or suggest using columns “pre-filled with a spherical and porous silica gel having particle size between 3 and 45  $\mu\text{m}$  and pores between 30 and 300 $\text{\AA}$ ” (Claims 7 through 10). Watanabe teaches placing the material to be analyzed “on a silica gel column (Fuji-Davidson’s microbead silica gel 4B 200/350 mesh)”

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(Watanabe, Page 2293, LH Col. Lines 38 – 40). 200 mesh is 74  $\mu\text{m}$  and 350 mesh is 42  $\mu\text{m}$ . Thus, the range of particles in Watanabe's stationary phase include many particles well outside of the claimed range of 3 to 45  $\mu\text{m}$ . That some portion of Watanabe's stationary phase are particles within the range does not negate that a most of the range of Watanabe's stationary phase is well-outside the claimed range. Therefore, Watanabe cannot be said to teach or suggest Applicant's claimed invention.

Kamegawa merely explains the pore size of Fuji-Davidson's microbead silica gel 4B to be 7.7nm. However, Kamegawa does not teach or suggest particles in the claimed range. Accordingly, Kamegawa also fails to teach or suggest the claimed invention.

Therefore, even if Watanabe and Kamegawa were to be combined as suggested, such a combination would fail to include a stationary phase as claimed in Claims 7 through 10. Therefore, Claims 7 through 10 are not obvious over the combination of Watanabe and Kamegawa.

Danishefsky et al. (US 2002/0058817 A1) in view of Sigma-Aldrich ("Silica Gel") (44 – 45)

Claims 1, and 2 were rejected under 35 USC 103(a) as unpatentable over Danishefsky in view of Sigma-Aldrich ("Silica Gel"). If the Examiner considers the rejection applicable to the claims as amended and the new claims, Applicant traverses the rejection.

The Sigma-Aldrich ("Silica Gel") reference points to the spec sheet for Silica Gel H4267. For the sake of clarity, Applicant refers herein to that silica gel as "Sigma-Aldrich H2467". This is but one of many types of silica gel materials available for chromatography from Sigma-Aldrich.

The Examiner pointed to the statement that "flash chromatography was performed using the indicated solvent on E. Merck silica gel 60 (40-63  $\mu\text{m}$ ) or Sigma H-type silica gel (10-40  $\mu\text{m}$ )" Danishefsky, [0394] as a disclosure of "a column for flash chromatography comprising silica gel

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with a particle size between 40 and 63 micrometers” (Office Action, Page 10, Numbered Paragraph 45). The Examiner admits to that “Danishefsky does not explicitly disclose the silica gel being spherical or having pores with a size between 30 and 300 angstroms” (Office Action, paragraph spanning Pages 10 and 11). The Examiner asserts that Sigma-Aldrich (Sigma-Aldrich, “Silica Gel” demonstrates that to be spherical silica gel. Applicants disagree. Sigma-Aldrich supplies many types of silica gel. Sigma-Aldrich H2467 is not the closest material to that used in Danishefsky. The closest silica gel with a specification matching the disclosure of Danishefsky is Sigma-Aldrich S6628 (Sigma-Aldrich, “S6628 Silica Gel”, [http://www.sigmaaldrich.com/catalog/ProductDetail.do?N4=S6628%7CSIAL&N5=SEARCH\\_CONCAT\\_PNO%7CBRAND\\_KEY&F=SPEC](http://www.sigmaaldrich.com/catalog/ProductDetail.do?N4=S6628%7CSIAL&N5=SEARCH_CONCAT_PNO%7CBRAND_KEY&F=SPEC), accessed on April 20, 2010, attached hereto as Exhibit C). The spec sheet for this product reveals that it is Type H and has a particle size of 10 – 40 µm. Thus, it is a perfect match for the material disclosed by Danishefsky. The spec sheet does not reveal the shape of the particles. However, the undersigned has made an inquiry with Sigma-Aldrich and obtained the response from Dr. Ian Brockie, Ph.D./Senior Technical Service Scientist attached as Exhibit D indicating that S6628 is *irregular* shaped silica. Therefore Danishefsky explicitly teaches the use of a silica gel having *irregular* shaped particles.

For the foregoing reasons, Applicant respectfully posits that Danishefsky does not teach or suggest using a spherical silica as suggested by the Examiner. Therefore, Claims 7 through 10 are patentable over Danishefsky in view Sigma-Aldrich (“Silica Gel”).

Still et al. (J. Org. Chem.) in view of Sigma-Aldrich (“Silica Gel”) (46 – 46)



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Claims 1 and 2 were rejected under 35 USC 103(a) as unpatentable over Still in view of Sigma-Aldrich ("Silica Gel"). If the Examiner considers the rejection applicable to the claims as amended and the new claims, Applicant traverses the rejection.

The Sigma-Aldrich ("Silica Gel") reference points to the spec sheet for Silica Gel H4267. For the sake of clarity, Applicant refers herein to that silica gel as "Sigma-Aldrich H2467". This is but one of many types of silica gel materials available for chromatography. Applicant does not claim the invention of a particular silica gel. Applicant has invented the use of "a *spherical [and semi-spherical]* and porous silica gel having particle size between 3 and 45  $\mu\text{m}$  and pores between 30 and 300 $\text{\AA}$ " in flash chromatography.

Still is the seminal reference for flash chromatography. While Still describes flash chromatography and the use of silica gel as the stationary phase, Still does not teach or suggest using a "column pre-filled with a spherical and porous silica gel having particle size between 3 and 45  $\mu\text{m}$  and pores between 30 and 300 $\text{\AA}$ " (Claims 7 through 10). The Examiner acknowledges that "Still does not explicitly disclose the silica gel being spherical or having pores with a size between 30 and 300 angstroms (Office Action, page 11, Numbered paragraph 47). The Examiner proposes that Sigma-Aldrich H2467 stands for the proposition that Still teaches use of spherical silica (Office Action, Page 11, Numbered paragraph 47). However, that is not correct. Rather, Still proposed using "dry 40 – 63  $\mu\text{m}$  silica gel (E. Merck No. 9385)". Still, Page 2924, LH Col., Lines 10 – 11. Therefore, the reliance of Sigma-Aldrich H2467 for the missing teaching is improper.

E. Merck No. 9385 (Sigma-Aldrich, 227196 Silica Gel, [http://www.sigmaaldrich.com/catalog/ProductDetail.do?lang=en&N4=227196|SIAL&N5=SEARCH\\_CONCAT\\_PNO|BRAND\\_KEY&F=SPEC](http://www.sigmaaldrich.com/catalog/ProductDetail.do?lang=en&N4=227196|SIAL&N5=SEARCH_CONCAT_PNO|BRAND_KEY&F=SPEC), accessed on April 20, 2010, attached hereto as Exhibit E) is sold by Sigma-

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Aldrich. The spec sheet for E. Merck No. 9385 does not reveal the shape of the particles in E. Merck No. 9385. However, the Merck ChromBook 2008|2009 book describes the same product as being irregular. Merck, ChromBook 2008|2009, Pages 184 – 185, <http://www.merck-chemicals.com/showBrochure?id=200803.023>, accessed on April 22, 2010, excerpt attached as Exhibit F). Therefore Still explicitly teaches the use of a silica gel having *irregular* shaped particles.

For the foregoing reasons, Applicant submits that reading the specification of Sigma-Aldrich H2467 into Still is improper and the Still teaches the use of an irregular shaped silica. Accordingly, Claims 7 through 10 are not obvious over the proposed combination of Still and Sigma-Aldrich H2467.

#### Conclusion with respect to the Independent Claims

For the foregoing reasons, Claims 7 through 10 are patentable over the cited references and should be allowed.

#### Dependent Claims

Independent Claims 7 through 10 are argued as patentable over all the cited references. Claims 3 through 6, and 11 depend from the independent claims

Thus, for the reasons given above, Applicants respectfully request reconsideration of the claims and their early allowance.

The application is now deemed to be in condition for allowance and notice to that effect is solicited.

### CONCLUSION

It is submitted that all of the claims now in the application are allowable. Applicants respectfully request consideration of the application and claims and its early allowance. If the Examiner believes that the

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prosecution of the application would be facilitated by a telephonic interview, Applicants invite the Examiner to contact the undersigned at the number given below.

Applicants respectfully request that a timely Notice of Allowance be issued in this application.

Respectfully submitted,

Date: April ~~NNN~~, 2010

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